

IN THE CLAIMS:

Applicants, pursuant to 37 C.F.R. § 1.121, submit the following amendments to the claims:

1. (Original) A method for detecting, or detecting and distinguishing between or among colorectal cell proliferative disorders, comprising contacting genomic DNA of a biological sample obtained from the subject with at least one reagent, or series of reagents that distinguishes between methylated and non-methylated CpG dinucleotides within a target sequence of the genomic DNA, wherein the target sequence comprises a sequence of at least 18 contiguous nucleotides of a sequence selected from the group consisting of SEQ ID NOS:1-39.

2. (Currently amended) The ~~[[A]]~~ method of according to ~~claim 1~~, wherein said colorectal cell proliferative disorders are selected from the group consisting of colorectal carcinoma, colon adenomas, and colon polyps.

3. (Currently amended) The method of according to ~~claim 1~~, wherein the biological sample obtained from the subject is selected from the group consisting of histological slides, biopsies, paraffin-embedded tissue, bodily fluids, stool, blood, serum, plasma and combinations thereof.

4. (Currently amended) The ~~[[A]]~~ method of according to ~~Claim 1~~, comprising:

a) obtaining a biological sample containing genomic DNA;

b) extracting, or otherwise isolating the genomic DNA;

c) digesting the genomic DNA of b) comprising at least one CpG dinucleotide of a sequence selected from the group consisting of SEQ ID NOS:1-39, with one or more methylation sensitive restriction enzymes;

d) detecting the DNA fragments generated in the digest of c); and

e) determining, based at least in part on the presence or absence of, or on a property of said fragments, the methylation state of at least one CpG dinucleotide sequence of SEQ ID NO:1 to SEQ ID NO:39, or an average, or a value reflecting an average methylation state of a plurality of CpG dinucleotide sequences of SEQ ID NOS:1 to SEQ ID NO:39, whereby at least one of detecting, or detecting and distinguishing between or among colorectal cell proliferative disorders is, at least in part, enabled.

5. (Currently amended) The ~~[[A]]~~ method of according to ~~claim 4~~, wherein the DNA digest is amplified prior to d).

6. (Currently amended) The [[A]] method ~~of according to~~ claim 1, comprising:

a) obtaining, from a subject, a biological sample having subject genomic DNA;

b) treating the genomic DNA, or a fragment thereof, with one or more reagents to convert 5-position unmethylated cytosine bases to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization properties;

c) contacting the treated genomic DNA, or the treated fragment thereof, with an amplification enzyme and at least two primers comprising, in each case, a contiguous sequence at least 18 nucleotides in length that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NOS:40-195, and complements thereof, wherein the treated DNA or a fragment thereof is either amplified to produce one or more amplicates, or is not amplified; and

d) determining, based on the presence or absence of, or on a property of said amplicate, the methylation state of at least one CpG dinucleotide of a sequence selected from the group consisting of SEQ ID NOS: 1-39, or an average, or a value reflecting an average methylation state of a plurality of said CpG dinucleotide sequences, whereby at least one of detecting, or detecting and distinguishing between or among colorectal cell proliferative disorders is, at least in part, enabled.

7. (Original) The method of claim 6, wherein in b) treating the genomic DNA, or the fragment thereof, comprises use of a solution selected from the group consisting of bisulfite, hydrogen sulfite, disulfite, and combinations thereof.

8. (Original) The method of claim 6, wherein treating in b) comprises at least one of treatment subsequent to embedding the DNA in agarose, treating in the presence of a DNA denaturing reagent, or treating in the presence of a radical trap reagent.

9. (Currently amended) The method of claim 5 ~~any one of claims 5 or 6~~, wherein contacting or amplifying comprises use of at least one method selected from the group consisting of: use of a heat-resistant DNA polymerase as the amplification enzyme; use of a polymerase chain reaction (PCR); generation of a amplicate nucleic acid molecule carrying a detectable labels; and combinations thereof.

10. (Original) The method of claim 9, wherein the detectable amplicate label is

selected from the label group consisting of: fluorescent labels; radionuclides or radiolabels; amplificate mass labels detectable in a mass spectrometer; detachable amplificate fragment mass labels detectable in a mass spectrometer; amplificate, and detachable amplificate fragment mass labels having a single-positive or single-negative net charge detectable in a mass spectrometer; and combinations thereof.

11. (Original) A nucleic acid comprising a sequence of at least 18 contiguous nucleotides of a treated genomic DNA sequence selected from the group consisting of SEQ ID NOS:40-195, and sequences complementary thereto, wherein the contiguous sequence comprises at least one CpG, TpA, or CpA dinucleotide, and wherein the treatment is suitable to convert at least one unmethylated cytosine base of the genomic DNA sequence initially to uracil or another base that is detectably dissimilar to cytosine in terms of hybridization.

12. (Original) An oligomer or peptide nucleic acid (PNA)-oligomer, said oligomer comprising in each case a sequence of at least 9 contiguous nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a treated genomic DNA sequence selected from the group consisting of SEQ ID NOS:40-195, and sequences complementary thereto.

13. (Original) The oligomer of claim 12, wherein the contiguous sequence includes at least one CpG, TpG or CpA dinucleotide.

14. (Original) The oligomer of Claim 13, wherein the cytosine of the CpG, the thymine of the TpG, or the adenosine of the CpA dinucleotide is located at about the middle third of the oligomer.

15. (Original) A set of oligomers, comprising at least two oligomers according, in each case, to any one of claims 12 to 14.

16. (Original) The set of oligomers of Claim 15, comprising one or more oligomers suitable for use as primer oligonucleotides for the amplification of a DNA sequence selected from the group consisting of SEQ ID NOS:40-195, and sequences complementary thereto.

17. (Original) The set of oligomers of Claim 15, wherein at least one oligomer is bound to a solid phase.

18. (Currently amended) A use Use of the set of oligomers according to any one of

Claims 15 through 17, wherein at least one oligomer can be used as a probe for detecting at least one of the cytosine methylation state, or single nucleotide polymorphisms (SNPs) within a sequence selected from the group consisting of SEQ ID NOS:1-39, and sequences complementary thereto.

19. (Original) An oligomer array, according to claim 17.

20. (Original) The array of claim 19, wherein the oligomers or peptide nucleic acid (PNA)-oligomers are arranged on a planar solid phase in the form of a rectangular or hexagonal lattice, or in a form substantially so.

21. (Currently amended) The array of claim 19 ~~any one of Claims 19 or 20~~, wherein the solid phase comprises a material selected from the group consisting of silicon, glass, polystyrene, aluminium, steel, iron, copper, nickel, silver, gold, and combinations thereof.

22. (Currently amended) A kit for detecting, or for detecting and distinguishing between or among colorectal cell proliferative disorders, comprising:

a)[[i]] at least one of a bisulfite reagent or a methylation-sensitive restriction enzyme;

b)[[ii]] at least one nucleic acid molecule or peptide nucleic acid molecule comprising, in each case, a contiguous sequence of at least 9 nucleotides that is complementary to, or hybridizes under moderately stringent or stringent conditions to a sequence selected from the group consisting of SEQ ID NOS:1-195, and complements thereof.

23. (Currently amended) A use ~~Use~~ of a nucleic acid according to any one of Claims 11 or 25, of an oligomer or PNA-oligomer according to any one of Claims 12 through 14, of a kit according to Claim 22, of an array according to any one of Claims 19 through 21, of a set of oligonucleotides according to any one of Claims 15 through 17, or of a method according to any one of claims 1 through 10, for classifying, distinguishing between or among, diagnosing or determining the predisposition for colorectal cell proliferative disorders.

24. (Currently amended) A use ~~Use~~ of a nucleic acid according to any one of Claims 11 or 25, of an oligomer or PNA-oligomer according to any one of the Claims 15 through 17, of a kit according to Claim 22, of an array according to any one of the Claims 19 through 21, of a set of oligonucleotides according to one of claims 15 through 17, or of a method according to any one of Claims 1 through 10, for the therapy of colorectal cell proliferative disorders.

25. (Original) An isolated treated nucleic acid derived from a genomic DNA sequence selected from the group consisting of SEQ ID NOS:1-39, and sequences complementary thereto, wherein the treatment is suitable to convert at least one unmethylated cytosine base of the genomic DNA sequence to uracil or to another base that is detectably dissimilar to cytosine in terms of hybridization.